Trinity Delta

Scancell

Outlook

A leader in antibody and vaccine oncology platforms

15 February 2023

Scancell is a clinical stage immunology specialist. It has two promising oncology vaccine platforms, Moditope and ImmunoBody, and two antibody technologies, GlyMab (anti-glycans) and AvidiMab, with the potential to treat many solid cancers, either as monotherapy or in combination. Modi-1, the first Moditope programme, is progressing in a Phase I/II trial targeting hard-to-treat tumours with results due through 2023. The lead ImmunoBody programme, currently SCIB1, is in a Phase II study in metastatic melanoma. The broad acting GlyMab antibodies are generating exciting preclinical data, which led to a partnering deal with Genmab. Further such deals are expected. AvidiMab technology will be increasingly employed to enhance avidity and potency. Updating our risk adjusted NPV lifts our Scancell valuation to £269.6m, or 32.9p/share, from £237.4m, or 29.1p/share, previously.

Year-end: April 30	2021	2022	2023E	2024E
Revenues (£m)	0.0	0.0	5.3	0.0
Adj. PBT (£m)	(17.7)	(11.9)	(17.6)	(24.0)
Net Income (£m)	(15.5)	(2.1)	(15.7)	(21.9)
EPS (p)	(2.28)	(0.25)	(1.93)	(2.68)
Cash (£m)	41.1	28.7	17.8	20.2
EBITDA (£m)	(8.6)	(12.6)	(13.8)	(20.2)

Source: Trinity Delta Note: Adjusted numbers exclude exceptionals

- **Moditope vaccine induces CD4 activation** The Moditope platform should achieve a value inflection during 2023 as the lead vaccine, Modi-1, initially generates safety data from the ongoing Phase I/II trial. This should be followed later in the year by the first, admittedly early, indications of efficacy in difficult cancers. Moditope is unique; it targets highly tumour-specific epitopes and induces CD4 cytotoxic T cells, with the consequent immune cascade eliciting a direct killing effect on cancerous cells. Significantly, the trial design also examines treatment with a CPI combination.
- **GlyMab is the lead antibody platform** The deal with Genmab for a preclinical antibody programme provides attractive economics but, more importantly, is material validation for the GlyMab platform. Management has successfully created five monoclonal antibodies targeting tumour-associated glycans. These are exquisitely tumour-specific and, in contrast to other approaches, have been shown in preclinical models to have high affinity and good potency. The plan is to progress two of these proprietary programmes into the clinic before seeking partners.
- **ImmunoBody and AvidiMab are also progressing** The ImmunoBody platform is set to be revitalised as the current Phase II trial, SCOPE, exploring SCIB1 in advanced melanoma, transitions to the AvidMab enhanced and optimised formulation known as iSCIB1+. This should provide improved potency and efficacy, as well as usefully rejuvenating patent life for ImmunoBody and showcasing AvidiMab's properties.
- **Execution is what will drive share appreciation** Updating our Scancell model sees our valuation rise to £269.6m, equivalent to 32.9p per share (from £237.4m and 29.1p per share). Key near- and mid-term catalysts will be delivery of encouraging clinical data, increasing visibility on clinical progress, and delivery of further commercial deals. Positive outcomes should boost investor sentiment materially.

Price	18.78p
Market Cap	£156.27m
Enterprise Value	£133.37m
Shares in issue	818.4m
12 month range	10.5p-29.4p
Free float	54.4%
Primary exchange	AIM London
Other exchanges	N/A
Sector	Healthcare
Company Code	SCLP.L
Corporate client	Yes

Company description

Scancell is a clinical-stage immuno-oncology specialist that has four broadly applicable technology platforms. Two are therapeutic vaccines, Moditope and ImmunoBody, and two are antibody based, GlyMab and AvidiMab.

Analysts

Lala Gregorek
lgregorek@trinitydelta.org
+44 (0) 20 3637 5043

Philippa Gardner
pgardner@trinitydelta.org
+44 (0) 20 3637 5043

Investment case

Four platforms: two vaccine and two antibody-based

Scancell is a clinical-stage immuno-oncology specialist. It was founded in 1996 as a spin-out of research led by Professor Lindy Durrant at the University of Nottingham. There are four distinct technology platforms that address oncology vaccines and antibodies: **Moditope** vaccine effects are mediated via CD4 pathways; **ImmunoBody** vaccines employ CD8 T cell pathways; the **GlyMab** platform generates high affinity anti-glycan antibodies; and **AvidiMab** can enhance the avidity of most antibodies. All the therapeutic platforms should have broad applicability in many forms of solid tumours. The ImmunoBody technology was also employed to create COVIDITY, a second generation COVID-19 vaccine. Scancell initially listed on PLUS in 2008, moving to AIM in 2010. Sizeable investment by Redmile in 2020 transformed Scancell's ability to fund its activities. Leading shareholders are Redmile (29.7%), Vulpes (14.4%) and Calculus Capital (5.6%). The company is based in Oxford and Nottingham and has >50 employees.

Valuation

A valuation of £269.6m, equal to 32.9p a share (27.4p diluted)

We value Scancell using a sum-of-the parts, where the NPV of the four technology platforms are summed and netted out against forecast operational costs, and risk-adjusted to reflect the stage of development, with the clinical stage platforms assigned higher success probabilities. Conservative assumptions are employed for factors such as timings of clinical studies, market launches, adoption curves, and patient penetration. The antibody platforms may arguably have higher commercial potentials, but their earlier stage means lower success probabilities are used. Despite our cautious approach, we value Scancell at £269.6m, equivalent to 32.9p per share (27.4p fully diluted).

Financials

Plenty of opportunities and funded to value inflection points

H123 results were boosted by the £5.3m upfront fee from the Genmab deal. This saw the operating loss reduced to £2.0m (H122: £5.4m), despite the higher costs as three clinical trials progress, which saw R&D costs rise to £4.9m (H122: £4.0m). G&A costs were £2.4m (H122: £1.9m) due mainly to an increased share option charge. The interest payable and finance expense lines are impacted by the accounting treatment of the CLNs (see later). The cash balance was £24.0m (FY22: £28.7m), with the cash runway extending through to Q1 2024.

Sensitivities

Oncology is a crowded and competitive segment

Scancell's technology platforms, especially the GlyMab antibodies, are at the earlier development stages and, inevitably, carry a higher risk profile. The immuno-oncology sector is increasingly crowded and competitive, with multiple players (ranging from large pharmaceutical groups to biotech companies and even well-funded academic centres) vying to develop the definitive breakthroughs. Equally, the usual industry risks associated with clinical trial results, navigating regulatory hurdles, ensuring sufficient financing is in place, partnering discussions and, eventually, the exit strategy, also apply.

Scancell: so much more than oncology vaccines

Scancell has assembled four novel technology platforms that split neatly into therapeutic vaccines, ImmunoBody and Moditope, and antibodies, GlyMab (anti-glycan mAbs) and AvidiMab. Whilst vaccines are the most advanced, with key clinical efficacy data expected during 2023 for both the lead Moditope and ImmunoBody programmes, it is the antibodies, notably GlyMabs, that we view as less well understood and certainly under-appreciated. The recent deal with Genmab, a highly respected antibody developer, serves to validate the GlyMab approach and suggests the direct and potent anti-tumour activity seen in preclinical models could translate to the clinic. The next 12 to 18 months should see multiple, diverse, clinical trial results, a number of which could be genuine value inflection points. Whilst not without risks, we believe the current share price fails to reflect the opportunities. Updating our rNPV-based model sees our Scancell valuation rise to £269.6m (32.9p/share), from £237.4m (29.1p/share).

Clinical data will define the value of the vaccine platforms

We described the changes in cancer treatments in previous notes (eg Outlook April 2022), detailing the importance of the tumour micro-environment (TME) and the seven steps in how the immune system normally recognises and kills abnormal cells. Checkpoint inhibitors (CPIs) have transformed clinical practice, but their success also highlights their failings. Because CPIs work by removing the "brakes" on the immune system, rather than directly boosting immune function, patients may also benefit from combination therapies that include immune-stimulatory elements. It is here that a therapeutic vaccine could act synergistically, and such thinking underpins why therapeutic cancer vaccines are back in vogue.

Modi-1 data will give indications of Moditope's potential role

Scancell has a lead programme from both the Moditope and ImmunoBody vaccine platforms in clinical trials. Modi-1 consists of three citrullinated tumour-associated peptides. The open label Phase I/II study, ModiFY, is flexible and sees Modi-1 used alone or in combination with CPIs in solid tumours, including triple negative breast (TNBC), ovarian, renal and head and neck (H&N) cancers. The first formal safety and immunogenicity results are expected shortly, with early efficacy data during 2023. We view positive data as a major value inflection point.

iSCIB1+ effectively reboots whole ImmunoBody platform

SCIB1, the lead ImmunoBody vaccine, is completing a Phase II trial for metastatic melanoma. The study now reflects changes in clinical practice and includes doublet therapy consisting of ipilimumab (Yervoy) plus nivolumab (Opdivo), and with pembrolizumab (Keytruda). The new protocol has also switched the delivery system from electroporation to the PharmaJet needle-free device. If successful, management intends to transition to iSCIB1+, an AvidiMab enhanced version of SCIB1, that should bring increased potency and extend patent life.

Antibody platforms are at earlier stages but hold much promise

However, we feel it is GlyMab, anti-glycan tumour directed antibodies, and AvidiMab, avidity and potency enhancer, that are under-appreciated. The GlyMab platform has generated five preclinical compounds with attractive, and promising, anti-tumour activities that are fostering industry interest. The recent deal with Genmab, worth up to $624m if successful, is valued confirmation of clinical and commercial potential. AvidiMab is employed in the COVIDITY programme, where recent results have validated AvidiMab as an immune response booster. Our rNPV model has to place more emphasis on later stage programmes, yet we believe these antibody platforms are likely to also provide material value inflection points.

Four platforms addressing antibodies to vaccines

Greater understanding of oncology leads to more combination approaches

Over the past decade, the role of the immune system in tumour initiation and progression has become better understood, as has the importance of the tumour microenvironment (TME). The recognition of the multiple, and subtle, interactions between the two has seen clinical research and, increasingly, therapy being switched from a tumour-centric to a TME-centric model. The principles underlying the cancer-immunity cycle were explored in our extensive April 2022 Outlook. This also covered how immunotherapy aims to identify and correct the imbalance so that the cycle becomes self-sustaining again; how, unfortunately, tumour cells appear to have intrinsic mechanisms to help evade anti-cancer therapies through bypassing every targeted step of the cycle; and how the research effort has shifted to identifying and developing combination regimens that will boost overall efficacy and limit treatment resistance but do so with manageable side-effects.

Exhibit 1: Scancell's pipeline of programmes funded with current resources

	Product	Indication	Research	Preclinical	Phase 1	Phase 2	Key outcomes
Vaccines	Modi-1	TNBC, ovarian, renal, head & neck					Safety & immunological data H2 2022 Efficacy data 2023/24
	Modi-2	Multiple, solid tumours					Enter the clinic H1 2024
	SCIB1/iSCIB1+	Late-stage melanoma					Completion of SCOPE trial H2 2024
	COVIDITY	Covid-19					Completion of the COVIDITY trial H1 2023
Antibodies	SC134 T cell bispecific	Small cell lung cancer					Enter clinic H1 2024
	SC2811 Stimulatory mAb	Any solid tumour					Lead candidate H1 2023
	GlyMab® Current & new	Multiple tumours					Validation and deals on current and new targets
	AvidiMab®	Any mAb target					Licensing deals

Source: Scancell

Four distinct platforms with broad applicability

In this report we focus on Scancell's four technology platforms, which can be classified into Antibodies (GlyMab and AvidiMab) and Vaccines (Moditope and ImmunoBody). The vaccine platforms are the most advanced, with three programmes at varying stages of clinical trials. The GlyMab (anti-glycan tumour directed antibodies) and AvidiMab (avidity and potency enhancer) platforms are at earlier stages of development. Exhibit 1 details the programmes that are underway and funded through to value inflection points with current resources.

Modi-1 clinical trial data expected throughout 2023

Modi-1, the lead programme of the Moditope platform, is progressing through the ModiFY Phase I/II study with safety and immunology data from the three initial cohorts expected shortly. Efficacy data from the expansion cohorts, evaluating Modi-1 with current standard of care in renal, head & neck, and triple negative breast cancers, will become available through 2023/24. For the ImmunoBody platform, the SCIB1 melanoma programme is transitioning to the improved iSCIB1+ construct, with the Phase II SCOPE study expected to complete in H225.

GlyMab antibodies: novel and highly differentiated

Glycan antibodies are a highly attractive, yet little known, field

Monoclonal antibodies (mAbs) have quietly transformed clinical care for many chronic treatment regimens, being involved throughout the patient journey from initial diagnosis to targeted treatments. Their highly prized specificity makes them particularly suited to precision applications and their ubiquity across many disciplines, from ground-breaking academic research through to consumer pregnancy tests, is testament to their value. However, almost all mAbs target specific peptides or proteins, with few notable exceptions such as dinutuximab (United Therapeutics' Unituxin), which binds to the glycan GD2 and is used to treat children with high-risk neuroblastoma.

Glycans are key elements in many biologic pathways

Yet carbohydrate binding antibodies, such as glycans, play key roles in biology; such endogenous antibodies recognise bacterial, fungal, and other microbial carbohydrates to prevent systemic infections and help maintain microbiome homeostasis. Their presence on proteins has major impacts on functions such as bioactivity, folding, trafficking, stability, half-life, signalling, and mediation of cell–cell interactions. Aberrant glycosylation is known to be a common feature of many cancers and plays crucial roles during virtually all steps of tumour genesis and progression. Such aberrant glycosylation may occur in both glycoproteins and glycolipids, leading to the formation of tumour-associated carbohydrate antigens.

Glycosylation changes in cancer are not simply random

Glycosylation has an important role in immune evasion…

Work on how tumours create an immune-suppressive environment (TME) and exploit selective modifications (immunoediting) to evade effective anti-tumour immune responses is clarifying the role of tumour glycosylation in immune evasion. Aberrant tumour glycosylation alters how the immune system recognises the tumour and also induces immunosuppressive signalling through glycan-binding receptors. Tumour cells exploit glycans in a similar manner to pathogens, using their typical "normal" formats and functions to disguise themselves, hijacking the immune system for their own benefit.

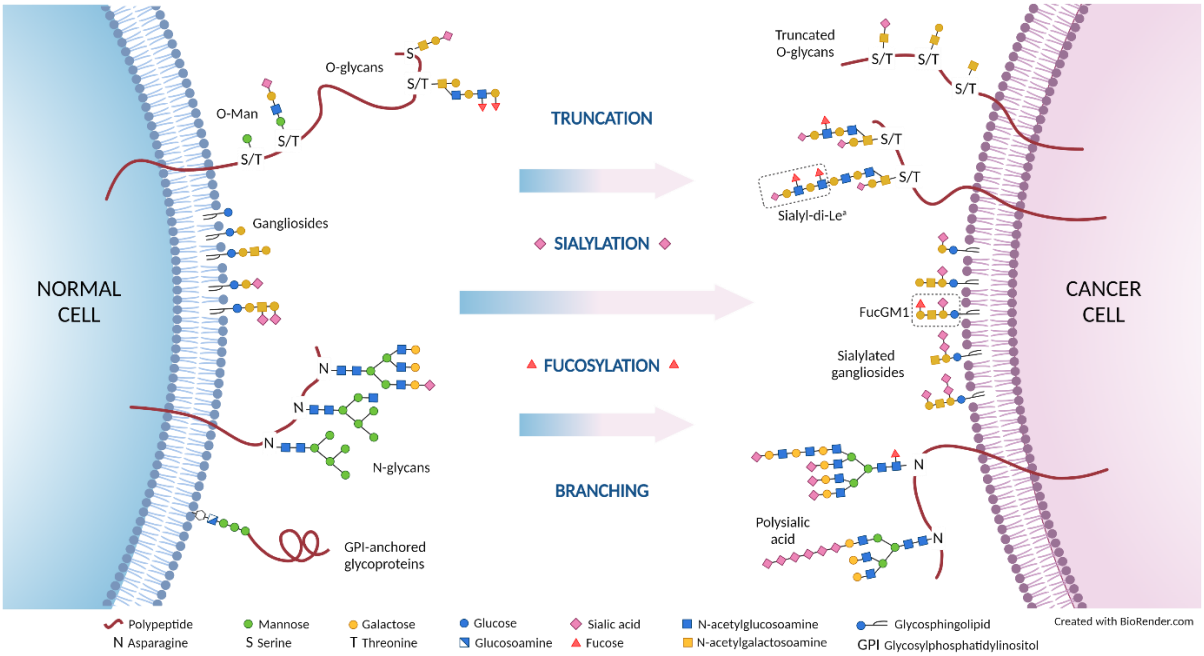
…malignancy, and tumour progression…

These glycosylation alterations take a variety of forms ranging from loss of expression or excessive expression of certain glycans, to increased expression of incomplete or truncated glycans, and, less commonly, the appearance of novel glycans. It is notable that these are not simply the consequence of disordered biosynthesis in cancer cells but highly specific changes that are correlated with malignant transformation and tumour progression. Given that cancer is a "micro-evolutionary" process in which only the fittest cells survive, and that tumours are under immune surveillance pressure, it is likely that these specific glycan changes have a functional role in tumour biology and are selected for during progression.

…and is associated with specific biologically relevant alterations

The key variations between a normal and cancer cell (Exhibit 2) include alterations to mucin expression and synthesis of incomplete or truncated O-glycans (encouraging pro-survival, migratory, and invasive behaviours), raised sialylation (a key step in cell fate decision), increased fucosylation (affecting adhesion molecules and growth factor receptors), and altered branching of N-glycans (profoundly involved in cancer growth, invasion and metastasis through pathways that are not yet fully understood).

Exhibit 2: Tumour cells and glycosylation



Source: Scancell

Glycans are attractive novel targets for tumour therapy

Although yet to be fully elucidated, such glycosylation is increasingly recognised as a modulator of the malignant phenotype of cancer cells, where the interaction between cells and the TME is altered to facilitate processes such as drug resistance and metastasis. The glycosylation of tumour proteins generates neo-antigens and these can serve as targets for tumour-specific T cells. The same glycol-epitopes can be present on a range of glycoproteins (GPs) and/or glycolipids (GLs).

Overcoming challenges as tumour therapeutic targets

Creating effective antibodies has been a major obstacle

Glycosylation is a post-translational modification that occurs inside the cell and results in the addition of glycans (sugar motifs) to proteins and lipids that are, in most cases, destined for the cell surface. These tumour-specific glycosylation patterns determine the immune-inhibitory properties of the tumour and are unlike those of normal cells, which in turn makes targeting of these glycans such an attractive therapeutic opportunity. The challenge has been to produce high affinity monoclonal antibodies that recognise tumour-associated glycans.

Specificity and immunogenicity are key hurdles to overcome

Carbohydrate structures are typically not highly immunogenic, unlike most proteins, and tend to result in the formation of IgM antibodies with low binding affinities that are not suitable for therapeutic use. Additionally, it is more difficult to identify and create glycan antibodies that bind specifically to a glycan of interest, in contrast to an antibody that binds explicitly to a protein epitope. Hence, although tumour-associated glycans are typically exquisitely tumour-specific, this explains the challenge in producing high affinity antibodies.

GlyMabs are highly selective, very effective and potent

The GlyMab platform has potentially overcome these limitations and is very flexible, consistent, reproducible, and potent. The technology stems from Scancell's in-house expertise and can be employed to produce many differentiated mAbs that bind selectively to the target tumour-associated glycans.

GlyMab platform potentially addresses key issues

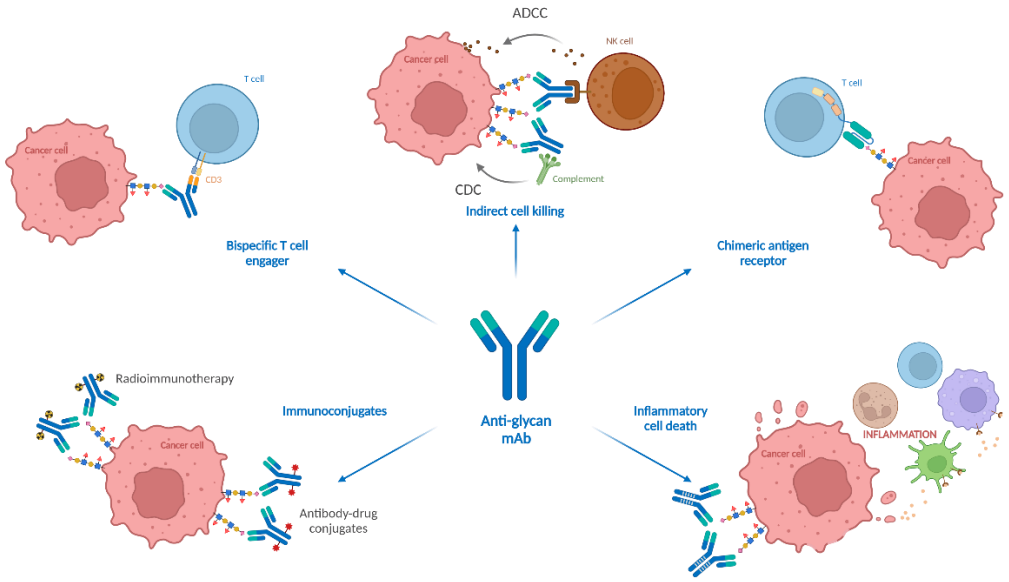
GlyMabs could potentially harness a wide array of actions

Preclinical studies have shown GlyMabs have high affinity for glycans which are highly over-expressed on cancer cells. These can directly lyse tumour cells by damaging the cell membrane (oncotic necrosis), without the need for the complement system or immune effector cells, through a form of immunogenic cell death (ICD) that plays a major role in stimulating the dysfunctional anti-tumour immune system. The resulting secretion of damage-associated molecular patterns (DAMPs) following ICD attracts receptors and ligands on dendritic cells (DCs) and initiates an immune response that should result in long-lasting protective anti-tumour activity. Potentially these anti-glycan mAbs can help remobilise the full arsenal of the immune system in an otherwise immunosuppressive environment.

Each target could generate multiple product types

The platform is highly flexible as these same glycans can be expressed by a wide range of proteins and lipids. This means each anti-glycan antibody can be developed into multiple products such as antibody drug conjugates (ADC), bispecific antibodies, chimeric antigen receptor T cells (CAR-T), redirected T cell killing both directly and indirectly (via ADCC antibody dependent cell cytotoxicity or CDC complement dependent cytotoxicity), or radioimmunotherapy (Exhibit 3).

Exhibit 3: Illustrations detailing the various killing mechanisms of glycan antibodies



Source: Scancell, Vankemmelbeke M et al; OncoImmunology 5:1; January 2016

Genmab deal provides potent validation of the whole thesis

Scancell has built a pipeline of differentiated anticancer mAbs and currently has five in early-stage development. In October 2022 Genmab effectively validated the GlyMab platform when it acquired the rights to develop one of these preclinical mAbs, SC129, into multiple novel therapeutic product modalities for all disease areas, excluding cell therapy applications (which are retained by Scancell).

SC129 licensed for ADC, TCB and radio-immunotherapy applications

SC129 is in lead candidate selection and targets sialyl-di-Lewis[a], with high selectivity for pancreatic tumours (74%), gastric cancers (50%) and colorectal cancers (36%). Genmab has licenced SC129 for antibody drug conjugates (ADC), T cell bispecifics (TCB), and radio-immunotherapy applications. Lewis-based glycans are attractive as they have a very limited distribution on normal tissues and are over-expressed in cancers that occur in epithelial cells. Preclinical testing has

shown strong binding affinities for the targeted tumour cells (pancreatic and gastric), with very limited binding to normal tissues. Direct and bystander killing effects were demonstrated by internal and external preclinical studies, including the assessments undertaken by Genmab.

Modest upfront and greater share of success upsides

The deal's potential value could reach up to a maximum of $624m if all the modalities were to be progressed, with Genmab paying Scancell an upfront payment of $6m and potential future milestones of up to $208m for each product. Scancell is also entitled to receive a low single digit royalty on net sales of all commercialised products. Genmab has a proven track record of successful clinical development and commercial execution. Importantly it has ample funds, which should enable rapid progression towards clinical trials.

Genmab is a respected, innovative, and successful mAb specialist

As context, Genmab is a Danish biotechnology company focused on developing innovative and differentiated antibody therapeutics. Its antibody expertise has resulted in five approved products, notably Darzalex for multiple myeloma, which is marketed by partner Johnson and Johnson (JNJ) and achieved sales of $7.98bn in 2022. In addition, Genmab has a broad pipeline of best- or first-in-class antibodies, which are based on in-house proprietary technology platforms and through strategic partnerships. Genmab aims to become a fully integrated biotech, and recently launched Tivdak for cervical cancer as part of a co-promote with partner Seagen. It is worth highlighting that Genmab is well capitalised, with > $3bn in cash and equivalents, and is sustainably profitable.

Four further wholly owned programmes progressing through preclinical development

Of the other four known programmes, a further three directly target solid tumours. Two are set to be taken into the clinic by Scancell:

- **SC134** is a redirecting T cell bispecific undergoing functional analysis and targets fucosyl GM1, with an initial focus on small cell lung cancer (SCLC). Fucosyl-GM1 is known to be expressed in up to 90% of SCLC and, unlike many other lung cancer antigens, has little or no expression in normal tissues. It is completing preclinical studies and is currently on target to enter the clinic in H224.
- **SC88** is in lead candidate selection and targets Lewis^{acx} with a view to addressing colorectal cancer. The cell-based studies again showed highly specific target binding with little off-target effects.
- **SC27** is in functional analysis targeting Lewis^{y} for gastric cancers. Preclinical studies have shown it to be more selective and potent than previous Lewis^{y} targeting approaches.
- The fifth mAb, **SC2811,** is a mAb that stimulates tumour infiltrating T cells. It is undergoing target validation for glycolipid stage-specific embryonic antigen 4 (SSEA4) on human and mouse T stem memory cells. It could have clinical value in many solid tumours. An AvidiMab modified ultra-specific lead candidate is expected to be selected during H123.

Visibility on partnering progress expected to be low

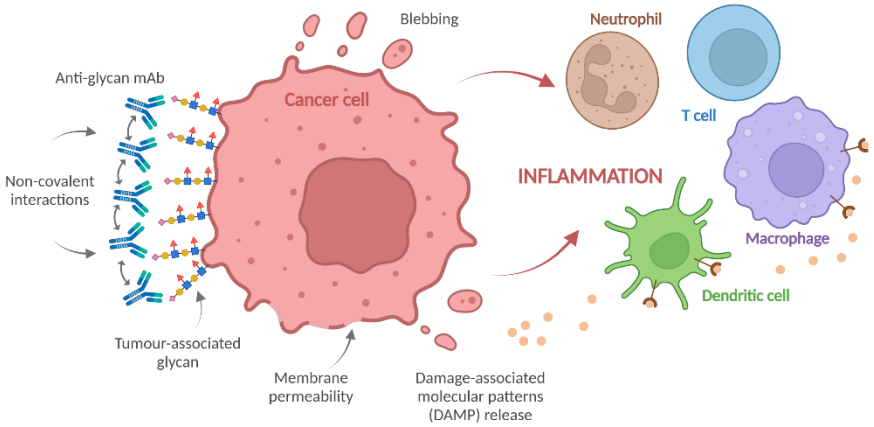
We expect the remaining programmes, and other undisclosed ones in earlier stages of preclinical development, will be progressed to preclinical validation points and then also be partnered for further clinical development. The nature of these developments suggests there will be few public indications of likely timings, with partnering progress visibility largely dependent on company disclosure.

AvidiMab: improving immune responses

Able to enhance the avidity of any antibody

The AvidiMab platform can enhance the avidity and potency of any antibody. It is based on specific modifications to the Fc domain of the antibody that result in non-covalent interactions between adjacent Fc regions. The findings arose as part of academic work on glycan antibodies to explore why activity was lost in certain settings. A series of constant region shuffling and subdomain swapping identified the Fc regions involved, with the discovery that introduction of selected residues resulted in retention of the desired effector functions and not only maintained activity but increased it. The initial work was carried out at Nottingham University, with Scancell acquiring the original IP and all rights to the AvidiMab technology in April 2018. Subsequent in-house work has further improved activity, broadened applicability, and created additional IP.

Exhibit 4: AvidiMab mechanism of action



Source: Scancell

Wide applicability across any mAb or similar protein structure

The AvidiMab platform is based on the observation that the mouse IgG3 glycan-targeting mAb often induces direct cell killing in the absence of immune effector cells or complement through a pro-inflammatory mechanism that resembles oncotic necrosis. This was identified as due to a non-covalent association between the Fc regions of neighbouring antibodies, with the inter-molecular cooperativity resulting in enhanced functional affinity and direct tumour cell killing. The effect is caused by key unique sequence residues that are present in the mouse but not seen in the equivalent human antibodies. Essentially AvidiMab can transfer these active residues to any target humanised antibody and so enhance non-covalent interactions between any mAb (or similarly structured) molecules resulting in a material improvement in avidity and potency.

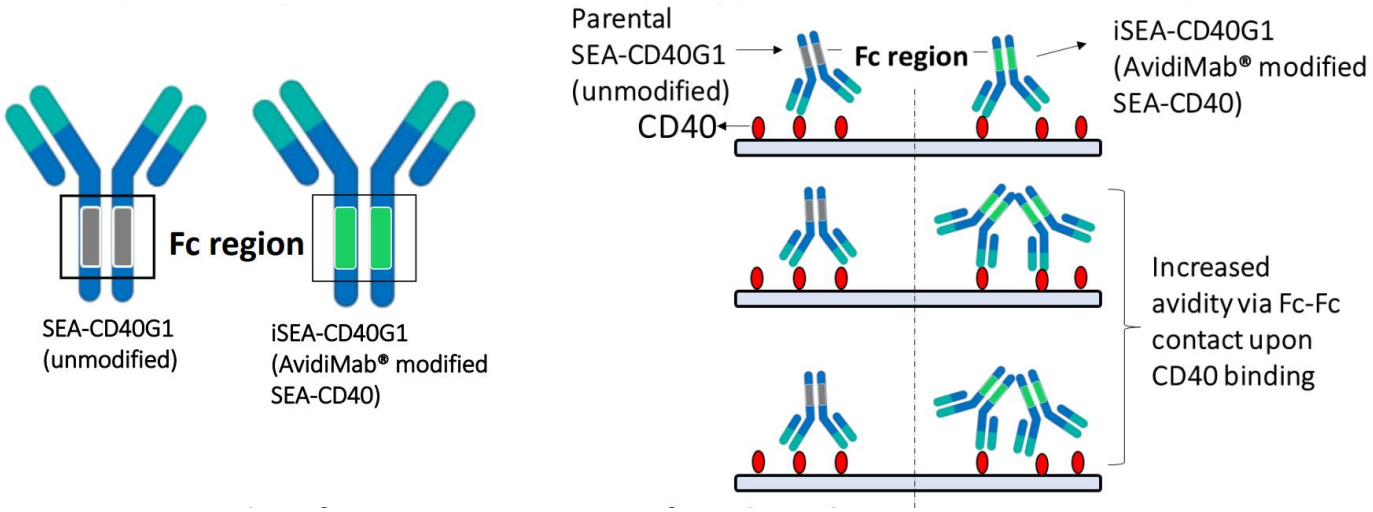
Exploiting Fc-Fc interactions to improve the therapeutic index

Antibodies are typically described as Y shaped molecules that contain two identical Fab (fragment antigen binding) arms coupled through a hinge to an Fc (fragment crystallisable) domain. The Fab arms provide specificity and mediate target antigen binding, whilst the Fc enables engagement with immune effector functions. Although Fab domains can be therapeutically active, for the majority of effector functions it is Fc that is key. The manner in which Fc interacts can also materially affect an antibody's therapeutic profile, for instance prolonging half-life and improved binding. Some of the preclinical work on a CD40 antibody enhanced with AvidiMab (named iSEA-CD40) has been presented in two poster sessions (September 2022 and November 2022).

Promising activity in CD40 based preclinical models

CD40 (cluster of differentiation 40) agonists are a promising area in immuno-oncology as they increase the number and quality of tumour-infiltrating T cells. Theoretically they should be highly effective as a monotherapy or to reverse resistance to checkpoint-blocking antibodies. However, preclinical potency has not yet been replicated in the clinical setting and none of these mAbs have advanced beyond early trial phases. One of the challenges encountered was insufficient immune activation, which resulted in antitumor efficacy only becoming apparent at toxic doses.

Exhibit 5: How AvidiMab Fc engineering technology acts to improve binding in SEA-CD40G1 model



Source: Scancell (Bubacarr G Kaira et al, 2022)

SEA-CD40 (Seagen) is in Phase II trials for advanced solid tumours. AvidiMab was used in the Fc region (Exhibit 5) in an IgG1 format, with key residues from murine IgG3 transferred into the human SEA-CD40 IgG1 Fc region. The results for iSEA-CD40 showed higher Fc-Fc self-association, slower off-rate and improved binding to CD40, and better functional affinity than original SEA-CD40. These findings of better performance were also seen in other immune models that rely on clustering and/or increased residence time for activity. Preclinical work continues to highlight the versatility and broad applicability of the AvidiMab platform, with sizable improvements seen across many applications.

iSCIB will provide important validation for AvidiMab

AvidiMab technology has been applied to Scancell in-house programmes, notably the anti-glycan mAbs to improve their ability to directly kill tumour cells, without mediation by other elements of the immune system. The AvidiMab platform has also been used to increase the potency of the T cell response in the COVIDITY vaccine programme and, in turn, to the SCIB oncology programmes (named iSCIB, where i stands for improved). With the ImmunoBody vaccines AvidiMab improves the breadth of response, increases potency, provides better long-term protection and immunological memory, and extends patent lifetimes. These programmes should produce evidence of the clinical value AvidiMab provides and could lead to its application in external programmes.

Moditope: a highly innovative vaccination approach

Therapeutic cancer vaccines are coming into vogue

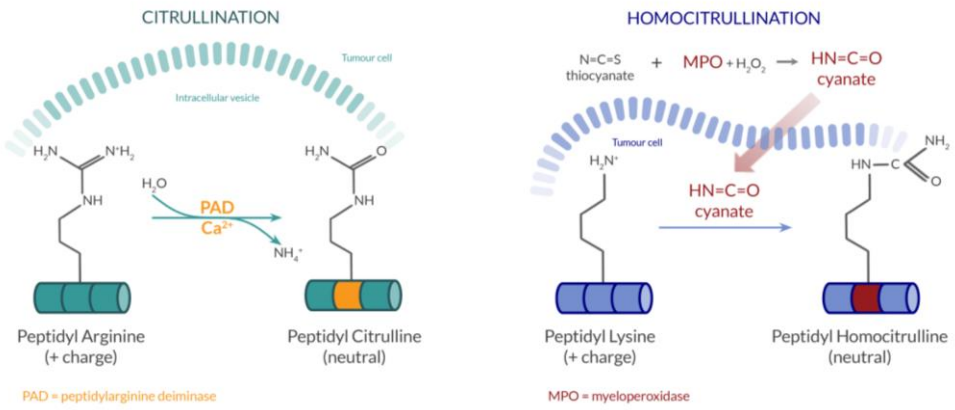
We have previously mentioned how therapeutic cancer vaccines appear to be following a similar pattern to that seen historically with monoclonal antibodies as immunotherapies, and it is clear that interest in such vaccines has undergone a resurgence in the past decade. In part this is driven by a better understanding of the cancer immunity cycle but, arguably just as importantly, improved vaccine design. This has been helped by a better understanding regarding the breadth of tumour-associated antigens, the native immune response, and the development of new technologies for antigen delivery.

Exploiting pathways connected to stressed tumour cells

A novel mechanism that is highly selective for tumour cells

Moditope is a novel approach that targets the modified self-antigens induced by cellular stress and exploits the normal immune responses that remove such stressed cells. Unregulated proliferation and the nature of the TME means cellular stress is common in solid tumours; most cancer cells are hypoxic and nutrient deficient. To help survive in this hostile environment, autophagy occurs to recycle unwanted proteins and dispose of damaged ones that could become toxic. Autophagy is highly localised in the centre of a growing tumour, prior to the occurrence of angiogenesis (which stimulates blood vessel formation). During this process, stress-induced post-translational modifications (siPTMs) of proteins and proteolytic cleavage occurs, which results in a selectively higher concentration of these modified peptides within the tumour than in normal tissues (as normal cells are rarely stressed in these ways).

Exhibit 6: Schematic of the citrullination and homocitrullination pathways



Source: Scancell, Seminars in Immunology VA Brentville 2020

Citrullination results from autophagy induced in stressed cancer cells

PTMs are mediated by multiple enzymes, some of which are only dysregulated in tumour cells, making them potentially highly tumour-specific. Citrullination, an enzyme driven conversion of arginine to citrulline, and homocitrullination (or carbamylation), where lysine residues are converted to homocitrulline, are examples of such tumour localised stress induced PTMs (Exhibit 6). Citrullination is mediated by activated PAD (peptidylarginine deiminase) enzymes, a family of calcium-dependent enzymes found in a variety of tissues, that modify the digested protein fragments within autophagosomes and convert arginine residues to citrulline. Homocitrullination (or carbamylation) sees MPO (myeloid peroxidase) similarly converting lysine residues to homocitrulline. Citrullination and

homocitrullination are selectively raised in cancer cells as a direct result of the continuous environmental stresses and the increased autophagy associated for cancer cells within the TME.

Pathway dysregulation still poorly understood, but neo-epitopes are what matter

The dysregulated citrullination pathways were initially linked to autoimmune diseases, mainly rheumatoid arthritis. The breadth and depth of the biological functions mediated by citrullination is still poorly understood (especially whether its effects are context driven). However, it is known to affect pathways directly contributing to cancer progression, specifically the Wnt/β-catenin and androgen receptor signalling pathways. It is also implicated in tumour progression, proliferation and metastasis through multiple mechanisms including EMT (epithelial-mesenchymal transition); it influences fundamental cellular processes such as apoptosis and differentiation; it facilitates the entrapment of circulating cancer cells at distant sites; and is associated to the awakening of dormant cells.

Unusually, these stimulate a potent CD4+ response, not the typical CD8+ one

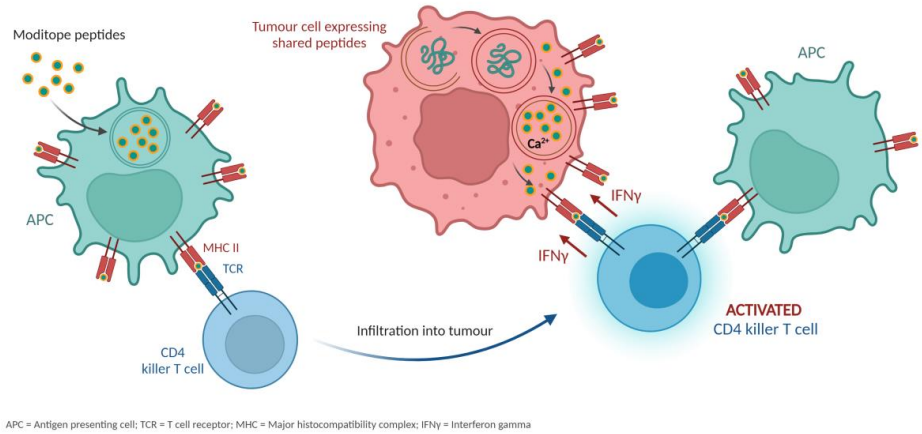
These citrullinated proteins are promising antigens for tumour targeting therapies, with α-enolase (ENO1), vimentin (VIM), nucleophosmin (NPM1), matrix metallo-proteinase-21 (MMP21), cytochrome p450 (Cp450), and glutamate receptor ionotropic (GRI) citrullinated peptides being explored in a range of solid tumours. Typically, the MHC (major histocompatibility complex) I peptides, presented to CD8+ or killer T cells, are generated by proteasomal degradation of intracellular proteins. In contrast, MHC II bound peptides, presented to CD4+ or helper T cells, derive from extracellular antigens, phagocytosed by APCs and degraded by lysosomal proteolysis. Importantly, these neo-citrullinated peptides are processed through the MHC-II pathway and present for the direct recognition of stressed cells by cytotoxic CD4 T cells.

Achieving the induction of high-avidity, cytotoxic T cells

Moditope could offer high potency with few side-effects

The Moditope platform neatly harnesses the normal immune response that uses cytotoxic CD4 T cells to eradicate stressed cells. It is now known immunisation with citrullinated proteins induces long-lasting CD4 T cell responses to tumour cells and, importantly, T cells recognising citrullinated epitopes have no target on normal healthy cells (the effect on cells involved in autoimmune diseases is not believed to be significant).

Exhibit 7: The mechanism of action of the MODI-1 vaccine



Source: Scancell

A four-stage process in creating a tumour killing cycle

Exhibit 7 illustrates how the Moditope platform works, using Modi-1 as the example. Citrullinated (or homocitrullinated) peptides are directly conjugated to adjuvant to activate APCs. The citrullinated peptides are taken up, processed, and presented on MHC class II molecules on the APCs. The CD4 T cell receptors bind to the MHC class II molecules and are primed. These CD4 T cells infiltrate the tumour environment, encounter, and recognise the citrullinated peptides expressed on the APCs. The CD4 T cells become activated and release IFN-ϒ, which induces upregulation of MHC II expression by tumour cells. CD4 cells become further activated and kill tumour cells.

Can be used as monotherapy or in combinations as appropriate

Tumour cells typically create a protective anti-inflammatory micro-environment (TME), where MHC II expression is not upregulated, to evade the immune system's normal response. The secretion of IFN-ϒ and the resultant inflammation could alter the nature of the TME, effectively converting "cold" tumours into "hot" ones, making a tumour visible to other elements of the immune system. Hence, Moditope stimulates the production of killer CD4 T cells which overcome the immune suppression induced by tumours, allowing activated T cells to seek out and kill tumour cells that would otherwise remain hidden from the immune system. This suggests Moditope offers the scope to be used alone, or in combination with other agents (including checkpoint inhibitors), to treat a wide range of currently hard to treat cancers.

Exhibit 8: A comparison of characteristics of Moditope and standard therapeutic vaccines

Reason for limited efficacy	Moditope	Standard therapeutic vaccines
Antigens targeted	Common proteins (eg cytoskeletal proteins) that have post-translational modifications	Tumour-associated antigens or neo-antigens
T cell response	Cytotoxic CD4 T cell and CD4 Th cell	Cytotoxic CD8 T cell and CD4 Th cell
Synergistic with checkpoint inhibitors	Yes, although this may not be required	Yes
Delivery system	Peptide directly conjugated to adjuvant	DNA, RNA, unlinked peptides or virally encoded antigens

Source: Trinity Delta

Promising preclinical data across many hard-to-treat cancers

Scancell has identified, and patented, a series of these siPTM modified epitopes. Promising preclinical studies show Moditope can generate a potent immune response against many solid tumours. Animal studies using a variety of citrullinated and homocitrullinated peptide combinations confirmed the early work using cancer cell lines and have shown impressive survival in several aggressive tumour models. Interestingly, the effect appears to be long-lasting as tumour rechallenge assays show generation of a strong immune memory. The potency of the anti-tumour response seen suggests tumours have limited defences against an attack from cytotoxic CD4 T cells, unlike one from cytotoxic CD8 T cells.

Modi-1 entering key Phase I/II clinical study

Two approaches to Moditope vaccines under evaluation

Scancell is currently progressing two Moditope programmes: Modi-1 and Modi-2. The Modi-1 vaccine consists of two citrullinated vimentin peptides (Vim28 and Vim415) and a citrullinated enolase peptide (Eno241) and is entering Phase I/II clinical trials. Modi-2 is focused on the homocitrullination pathways and is in preclinical evaluations to optimise it for a number of solid tumours.

Modi-1, using citrullination, is the most advanced

Modi-1 is the lead vaccine candidate and is composed of two targeting proteins. The first is vimentin, a cytoskeletal protein that is preferentially digested during autophagy. Vimentin plays a pivotal role in EMT and is associated with regulation of attachment, migration, and signalling in many solid tumours. Mesenchymal tumours such as endometrial, renal, sarcomas, lymphomas, and lung tumours express vimentin as their major cytoskeletal protein and, additionally, many epithelial tumours, eg breast, ovarian, renal, head & neck, gastrointestinal and prostate, switch from expression of cytokeratin to vimentin during metastasis.

Targets are selected to maximise expected responses

The second target is α-enolase, a metalloenzyme involved in glycolysis, that contributes to cancer cell proliferation, migration, invasion, and metastasis. Typically, cancer cells rely on aerobic glycolysis (the Warburg effect) for energy production, even when oxygen is not deficient. α-enolase is overexpressed in a range of cancer types, and it plays a key role in regulating tumour metabolism, proliferation, and survival in cancers such as ovarian, renal, head & neck, lung, pancreatic and TNBC, making it attractive as a vaccine target.

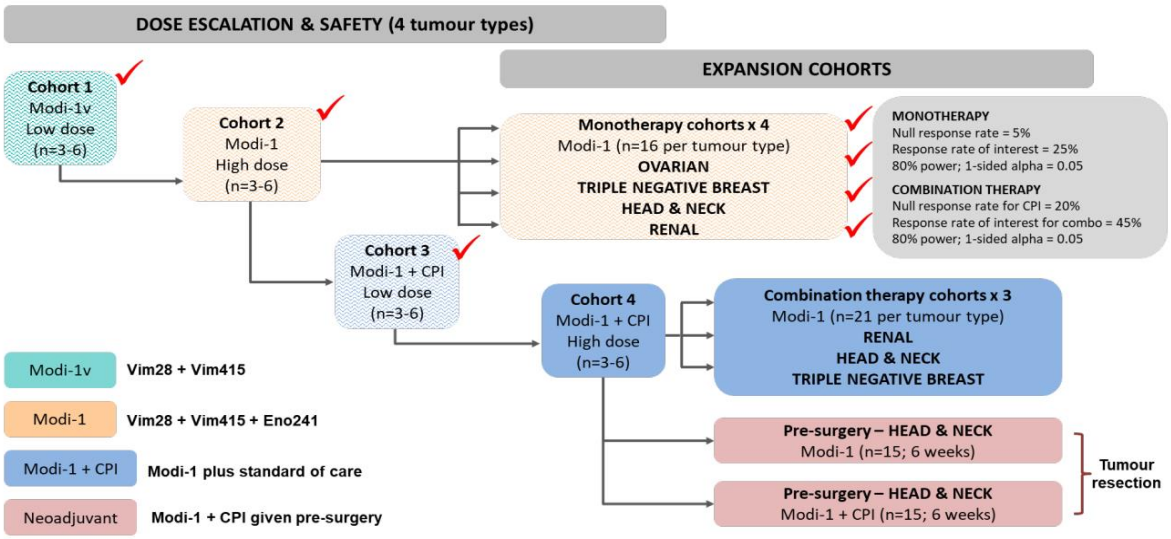
Appropriate adjuvant improves the vaccine's activity

Modi-1 employs three citrullinated peptides, two derived from vimentin and one from α-enolase, with the combination selected specifically to minimise the possibility of tumour escape. These are conjugated to a synthetic toll-like receptor (TLR) 1/2 agonist (AMPLIVANT, owned by ISA Pharmaceuticals), which acts as a potent adjuvant and materially enhances activity (10-100 fold) through better dendritic cell antigen processing and presentation plus enhanced T cell priming.

Issues with manufacture of novel components have been solved

Producing commercial quantities of these three conjugates posed a number of technical challenges, but these have been overcome. The data package, including toxicology, to support first-in-human trials was successfully completed and the Phase I/II clinical study format to explore safety, immunological activity, and preliminary efficacy agreed. The study started with the two citrullinated vimentin peptides (Vim28 and Vim415) and, as there were no local or systemic toxicities or side-effects, the citrullinated enolase peptide (Eno241) was added.

Exhibit 9: Modi-1 Phase I/II clinical trial design



Source: Scancell

Phase I/II study design selected to maximise understanding

The Phase I/II study (ModiFY) is two stage: an initial dose escalation and safety phase followed by a number of specific cohorts that explore for initial signs of efficacy in TNBC, ovarian cancer, head & neck cancer, and renal cancer (Exhibit 9). These will allow Modi-1 to be employed as both monotherapy and in combination with a CPI, as well as in the neoadjuvant setting. The patients will likely have failed their first line of therapy. This is, in our view, an important point as prior chemotherapy could stress normal cells and so, in theory, potentially impact Modi-1's selectivity for tumour cells (resulting in on-target off-tumour effects).

First two dose escalation cohorts completed, with the third now underway

The trial has been designed to provide insightful data in a variety of clinical settings. Up to 138 patients in up to 20 sites across the UK will be examined. Nine sites are actively recruiting with another three expected to initiate screening during 2023. To date, 21 patients have been dosed successfully and a further 16 recruited. Cohort 1 confirmed the safety profile of a low dose of the two vimentin peptides. Cohort 2 used these peptides plus an enolase peptide at a higher dose. All patients showed the injections are well tolerated with no safety concerns. One patient with head & neck cancer has shown a confirmed partial tumour response with further tumour regression at week 16. Two further patients have shown stable disease. To date, 13 ovarian, 2 breast and 3 head and neck patients have been dosed. Cohort 3 is currently underway and involves combination with a CPI. Further safety and immunological data are expected to be available through H123, with first signs of efficacy data likely later in 2023.

Modi-2 is exploring homocitrullination pathways

Modi-2 employs homocitrulline pathways

The Modi-2 vaccine is based on the same principles but employs tumour-associated peptide epitopes in which lysine residues are converted to homocitrulline. Extensive preclinical work has identified homocitrullinated epitopes derived from several proteins that generate potent T cell responses. These proteins include vimentin, aldolase, cytokeratin 8, immunoglobulin binding protein (BiP), nucleophosmin (NPM), α-enolase, β-catenin (Wnt pathways), and heat shock protein (HSP-60). These epitopes are formed through carbamylation pathways in an analogous manner to PAD for citrullination, with MPO (myeloid peroxidase) converting lysine residues to homocitrulline.

These proteins have proven links to many solid tumours and encouraging and prolonged efficacy has been seen in the relevant preclinical cancer models and in tumour-expression studies or similar, notably breast, colorectal, non-small cell lung, and prostate cancer. Efforts are now directed towards characterising and picking appropriate epitopes (provisionally aldolase A, cytokeratin 8, immunoglobulin binding protein, and vimentin) for selected tumours, targeting those with a particularly immune-suppressive TME.

Novel SNAPvax technology to overcome formulation issues

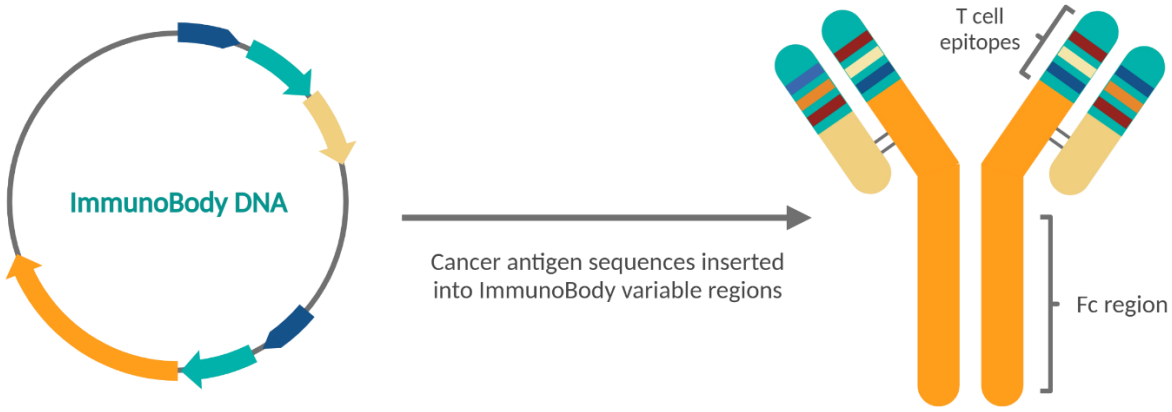
Modi-2 is planned to employ four homocitrullinated peptides that are conjugated to adjuvant and presented as micellar nanoparticles using the novel SNAPvax technology that was licensed in November 2022 from Vaccitech. SNAPvax enables peptides to self-assemble with TLR-7/8a, a powerful and proven adjuvant, to promote strong T cell responses and overcome the formulation issues that are often associated with immunogenic peptide antigens. The plan is to complete the non-clinical characterisation work, including manufacture, so that Phase I trials can start during H124.

ImmunoBody: CD8 T cells for a range of tumours

A versatile, flexible, and robust vaccine platform

The ImmunoBody platform creates DNA vaccines that encode a human antibody framework, but the parts of the antibody that would normally bind to the target protein, the complementarity determining regions (CDRs), are replaced with carefully selected cytotoxic T lymphocyte (CTL) and helper T cell epitopes from a cancer antigen (Exhibit 10). Each vaccine can be engineered with several selected cancer associated T cell epitopes to create a genetic antigen/antibody complex. The direct and cross presentation of antigens generates high avidity T cells with a broad and potent anti-tumour effect.

Exhibit 10: The structure of the ImmunoBody



Source: Scancell

A comprehensive immune response is activated

Therapeutic vaccines require targeting and activation of dendritic cells (DCs) to stimulate both CD4 and CD8 T cell responses. DCs are considered the most efficient APC (antigen presenting cells) being able to initiate, coordinate, and regulate adaptive immune responses. ImmunoBody constructs are flexible, but with core features that include:

- epitopes selected so they bind to both MHC I (for the CD8 T cell response) and MHC II (for the CD4 Th-cell response);
- an Fc region of the protein form that targets activated DCs.

Two complementary processes create high avidity responses…

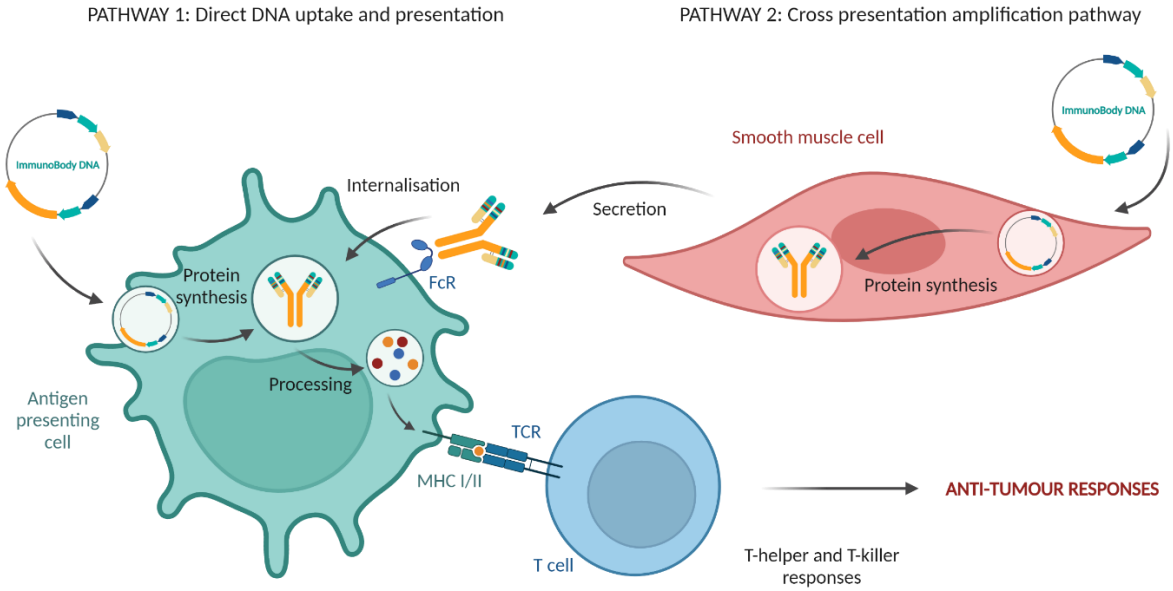
ImmunoBody vaccines activate DCs through two distinctly different and complementary mechanisms that maximise T cell activation and avidity: direct- and indirect/cross-presentation. There are various pathways by which DCs can process antigens, and the highest avidity T cell responses are generated if more than one pathway is used to present the same epitope.

…that should break through a tumour's defences…

Primarily, the DNA element is taken up directly by the DCs, via transfection, and the resulting protein is processed in the APC. This direct presentation produces the appropriate immune response but generates only moderate T cell avidity and the anti-tumour response is too weak in the typical immunosuppressed TME. However, an identical protein component is secreted by muscle cells (which is produced at the site of the injection from the DNA) that binds to the Fc receptors on DCs leading to the cross presentation of epitopes (Exhibit 11). This dual

approach generates both a cytotoxic CD8 cell response and a Th CD4 response that, importantly, is up to 100 times greater than either presentation alone with potent high avidity T cells generated. This amplified immune response is now sufficient to generate the required broad anti-tumour response in the TME.

Exhibit 11: The cross presentation of epitopes by ImmunoBody



Source: Scancell Note: TCR = T cell receptor; MHC = major histocompatibility complex; FcR = Fc receptor

...creating a positive and reinforcing mechanism

The ImmunoBody vaccines have been designed so that epitopes for both MHC I and MHC II complexes are produced once they have been broken down by the proteasome. Epitopes for MHC I are normally 8-11 amino acids in length and generate a CD8 response, and epitopes for MHC II are usually 13-17 amino acids long and result in a CD4 response. The generation of both a Th and Tc cell response is important, as the Tc cells only become activated and able to destroy the tumour cells once Th cells recognise the appropriate epitope and secrete cytokines and chemokines to activate and recruit T cells.

SCIB1: undergoing clinical trials in melanoma

SCIB1 clinical trials address metastatic melanoma

The lead ImmunoBody programme, SCIB1, is being developed for the treatment of metastatic melanoma. SCIB1 incorporates specific epitopes from the proteins gp100 and TRP-2, which were identified from the cloning of T cells from patients who achieved spontaneous recovery from melanoma skin cancers. Both proteins play key roles in the production of melanin in the skin.

First study produced potent and long-lasting responses

The original dose-escalation Phase I/II monotherapy study (SCIB1-001) in 35 patients with metastatic melanoma (Stage III and IV) showed a potent dose dependent T cell response in 88% of patients with no serious adverse events or dose limiting toxicities. Fifteen patients with tumours received SCIB1 doses of 0.4mg to 8.0mg, whilst 20 fully resected patients received doses of 2mg to 8mg. At the data cut-off point for the study, all 20 fully resected patients were alive, with a median observation time of 37 months from study entry. In the 16 patients with fully resected disease who received 2-4 mg doses of SCIB1, an impressive 14

were still alive five years after the study had started. Melanoma recurrence rates in resected SCIB1-treated patients were also lower than in historical controls.

Second Phase I/II study is in combination with CPIs

The second, and more recent, open label Phase II study (SCOPE) examines SCIB1 in combination with the CPI pembrolizumab (Merck's Keytruda) or the doublet therapy consisting of ipilimumab (Yervoy) plus nivolumab (Opdivo). The addition of the doublet cohort reflects changes in treatment regimens for metastatic melanoma. The study rationale is that the ImmunoBody vaccine primes an immune response against the tumour whilst the CPI reduces the immune-suppressant effect seen in the TME. Preclinical studies show a strong synergistic effect when SCIB1 is combined with a relevant CPI (c 85% response rates in animal models). The primary objectives are tumour response rate, progression-free survival and overall survival.

Delays have been unfortunate, but data are expected during 2023

The study was delayed by several factors, including COVID-19 related issues with clinical trial formats (affecting patient recruitment) and changes in standard of care for metastatic melanoma as mentioned. Under the updated protocol some 87 patients are expected to be treated up to 10 times for 85 weeks using the PharmaJet Stratis needle-free injection device system in the upper arm or upper leg. Eight trial sites are currently recruiting with a further six in the set-up stage. During 2023 the SCOPE study is expected to transition to dosing with iSCIB1+, a modified version of SCIB1.

iSCIB: pertinent use of AvidiMab to boost potency

AvidiMab modifications are key to iSCIB1+ improvements

The AvidiMab platform is being employed to increase effectiveness, and extend the patent life, of the ImmunoBody programmes. The initial work has been on modifying SCIB1 with additional epitopes also added. The effectively new programme is named iSCIB1+ and broadens utility to patients beyond those indicated with SCIB1. In addition to material improvements in potency, this allows it to be used to treat all patients rather than being limited to the 40% of patients who have the appropriate human leukocyte antigen (HLA) type. Preclinical work suggests that clinical benefits (in terms of performance, efficacy, and ease of administration) of iSCIB1+ are a significant advance over SCIB1.

AvidiMab used to revitalise the whole ImmunoBody platform

A similar reworking of SCIB2, where the published preclinical data showed promising results, has developed into a new programme known as iSCIB2. Again, the preclinical data suggest the AvidiMab modifications have resulted in excellent anti-tumour activity. Although we view these developments as new programmes, the existing experience (notably with manufacturing of clinical supplies and toxicology) with SCIB1 and SCIB2 means the iSCIB equivalents should progress more rapidly to the key clinical stages.

COVIDITY: first use of AvidiMab in the clinic

The COVIDITY programme, consisting of COVID-19 vaccine candidates SCOV1 and SCOV2, completed dosing in the South African studies and reported safety and immunogenicity data in February 2023. As previously communicated by management, this programme will not be taken forward in-house due to the competitive landscape but may be partnered. We had not viewed COVIDITY as a major element in Scancell's investment case, although it does provide useful evidence of AvidiMab's utility and proof of Scancell's vaccine creating skills.

Sensitivities

The science is appealing but the clinical risks are greater

Scancell operates at the cutting edge of immuno-oncology and the risks inherent in such research are higher than the industry average. The appeal of harnessing the body's immune system to treat tumours has attracted industry-wide attention, with multiple well-funded players operating in a crowded and competitive space. While Scancell's therapeutic platform technologies have demonstrable and attractive qualities, an unexpected breakthrough in an unrelated scientific area may side-line one or more of its approaches.

Operating in a crowded and highly competitive field

On the competitive front, both Moditope and ImmunoBody would be complementary to many methods under investigation to enhance the activity of the immune system, with combination therapies increasingly accepted as standard of care for many solid tumours. However, Scancell is also competing directly against other therapeutic vaccine companies, including collaborator BioNTech, and various companies developing oncolytic viruses. This is currently an area of particular interest to big pharma companies.

Genmab provides significant validation but earlier stage means risks are higher

The antibody platforms are at earlier development stages and, understandably, are riskier and more uncertain. GlyMab has generated genuinely exciting preclinical data, which has attracted a licensing deal from Genmab, but the potential value of the platform will only be realistically demonstrated in appropriate clinical trials. AvidiMab has broad applicability in enhancing antibody potency, however as yet there has been no third-party validation of its perceived worth.

Usual industry risks do apply and should not be under-stated

More generally, and in common with most innovative healthcare companies, the three main sensitivities relate to the clinical and regulatory aspects, the execution of the commercialisation plans (primarily partnership agreements), and the financial resources required to accomplish these:

- **Clinical aspects**: historic failures of previous therapeutic vaccines cloud expectations of Scancell's programmes. Yet Moditope and ImmunoBody both have different mechanisms of action to any prior attempts and should be judged on their own merits. The design and execution of the clinical programmes is an important determinant of any study outcome, but this is particularly the case in immuno-oncology trials (especially when evaluating differing therapies in combination).
- **Partnership/licensing and exit strategies:** the immuno-oncology field is particularly exciting, with many technologies attracting much scientific, and investor, attention. Against such a crowded and "noisy" background, it is always challenging for companies like Scancell to stand out sufficiently to attract the appropriate level of interest from potential partners. However, the expected availability of robust clinical data across multiple fronts should stimulate, and facilitate, industry interest.
- **Financial:** a common refrain is that European biotech companies are seldom financed appropriately to pursue their clinical ambitions in a timely manner. This was arguably true of Scancell historically; however, the material investment by Redmile in November 2020 means Scancell has sufficient resources (£24m at 31 October 2022) to progress its key programmes to attractive value inflection points.

Valuation

Updating our model sees our valuation rise to £269.6m, or 32.9p/share

Scancell can be viewed as a classic discovery play and so we employ a sum-of-the-parts model, where the risk-adjusted NPV of each platform is estimated (adjusted for the likely success probabilities), summed, and netted against operational costs. Success probabilities are based on standard industry criteria for the respective stage of the clinical development process but are flexed to reflect the inherent risks of the individual programmes, the technology risk, the indication targeted, and, where relevant, the trial design. As always, we use conservative assumptions regarding market sizes and growth rates, net pricing, adoption curves, and peak market penetration. The clinical programmes (including those ready to enter the clinic) carry the greatest weight, whilst preclinical programmes are discounted more aggressively to reflect the lower success probabilities. As is usual, our valuation has been updated to reflect financial results, FX, and has been rolled forwards in time. The key underlying assumptions for each platform are largely unchanged, unless described below, and are outlined in Exhibit 12.

Exhibit 12: Sum of the parts rNPV-based valuation of Scancell

	Total NPV (£m)	Likelihood of success	rNPV (£m)	rNPV/ share (p)	rNPV/ share diluted (p)	Notes
Moditope platform	1,220.0	10.0%	122.0	14.9	12.4	Peak sales: £3.5bn Royalties: 17.5% Launch year: 2029
GlyMab TaG antibodies	1,402.5	3.5%	50.3	6.1	5.1	Peak sales: £5bn Royalties: 17.5% Launch year: 2030 NB: includes Genmab deal
ImmunoBody platform	562.1	7.5%	42.2	5.2	4.3	Peak sales: £1.75bn Royalties: 17.5% Launch year: 2029
AvidiMab platform	1,450.5	2.0%	29.0	3.5	2.9	Peak sales: £8.5bn Royalties: 8% Launch year: 2030
Cash	26.2		26.2	3.2	2.7	Based on last reported and estimated cash burn
Total	**4,661.3**		**269.6**	**32.9**	**27.4**	
Discount rate				12.5%		
Exchange rate ($/£)				1.20		
Tax rate				10%		From 2029 (including Patent Box benefits)

Source: Trinity Delta

The four platforms all have value adding elements

The above table shows the various elements that make up our valuation. The vaccine platforms have greater visibility, and this determines their respective values. For the product-based elements, we use a blended royalty rate of 17.5% to reflect the typical upfronts and progress milestones that could form part of any future partnering deals. For AvidiMab we use a more modest 8% blended rate, which reflects the lower relative value-add, but offset to a degree by a broader applicability. Peak sales are estimated on the likely products and indications that each platform can generate. The current limited visibility means we have adopted conservative assumptions, arguably overly so, leaving the potential for future upside if progress materialises as management expects.

ModiFY additional efficacy data the next value inflection point for Moditope

The **Moditope** platform has a value of £122.0m, equivalent to 14.9p per share (12.4p fully diluted). The platform's next value inflection point should be from additional safety, immunogenicity and particularly efficacy data from the ongoing ModiFY Phase I/II study of Modi-1, which are expected during 2023. Modi-2 is expected to enter human trials in H124.

Valuation updated to include Genmab deal, which provides critical external validation

The **GlyMab antibody** portfolio consists of five preclinical programmes that could be employed in multiple differentiated product forms. The first partnering deal for one of these programmes was executed in October 2022 with Genmab. Scancell received an upfront payment of $6m and is entitled to future potential development, regulatory and commercial milestones of up to $624m for development across all modalities, with $208m for each product, plus single digit royalties on net sales. We have incorporated these deal terms within the GlyMab platform valuation. The Genmab deal provides external validation for the platform, and gives increased confidence in the platform's potential, in our view, hence we have increased the success probability to 3.5% for the yet to be partnered programmes (whilst maintaining other underlying assumptions on launch and peak sales) and apply a slightly higher 5% success probability to the Genmab partnered programme given the deal is now in place, which reduces execution risk. We value the portfolio of GlyMab antibodies, including the Genmab partnered programme, at £50.3m, equivalent to 6.1p per share (5.1p fully diluted).

ImmunoBody vaccine platform is transitioning to iSCIB construct

ImmunoBody now contributes £42.2m (from £53.6m), equivalent to 5.2p per share (4.3p fully diluted), as we have removed any contribution for COVIDITY in our peak sales. We continue to view the iSCIB programmes (SCIB programmes enhanced with AvidiMab) as relatively early stage despite a degree of validation provided by SCIB1's Phase I trial (first combination efficacy data is expected in 2023). Importantly, we view the true value inflection point as being when a suitable partner(s) takes iSCIB into the wider, and more expensive, clinical trials.

AvidiMab could have extensive industry appeal, but external validation is required

AvidiMab could be used to enhance the avidity and potency of virtually any antibody-based product. It would also extend the patent life of commercially established programmes. Hence its appeal could be significant. However, it has only been applied to Scancell programmes and until it has been licensed externally it is difficult to model with any degree of confidence. Consequently, we maintain a cautious approach, assuming the antibodies using AvidiMab technology have collective peak sales of £8.5bn. With this clear caveat, we value it at £29.0m, equivalent to 3.5p per share (2.9p fully diluted).

Our valuation is £269.6m, or 32.9p a share (27.4p diluted)

Summing the values of these platforms (with each incorporating associated costs) and adding our estimate for current cash resources (based on reported end-October 2022 cash of £24.0m less estimated cash burn, plus the Genmab upfront milestone receipt of £5.3m) we arrive at a valuation for Scancell of £269.6m, equivalent to 32.9p a share (27.4p fully diluted). There are a number of likely catalysts expected over the next 18 months, with successful outcomes expected to lead to upward revisions to our valuation.

Financials

Redmile investment released Scancell's brakes

Scancell's balance sheet was transformed in 2020, with the £30m Redmile investment boosting cash resources and enabling the three promising therapeutic platforms to progress effectively unhindered by funding concerns. End-October 2022 cash of £24.0m (April 2022: £28.7m), together with the $6m/£5.3m upfront payment from partner Genmab, underpins management's near-term plans to advance its leading programmes through the early clinical phases, and to develop the next wave of follow-on assets.

R&D spend continues to increase as platforms progress

Interim H123 financial results to end-October 2022, posted recently, were largely as expected. The non-recurring Genmab upfront payment of $6m/£5.3m was recognised in full in revenues (with cash received post period end). R&D spend increased to £4.9m (H122: £4.0m) with increased headcount and higher costs relating to development work on the Modi-1 clinical trial, and on the GlyMab and AvidiMab platforms. G&A expenses also rose, to £2.4m (H122: £1.9m), due to the higher stock option (non-cash) charge. Together, these led to an operating loss of £2.0m (H122: £5.4m loss).

CLN results in a number of non-cash items; prior period skewed by £7.2m accounting gain

Interest payable was £1.3m (H122: £1.7m), which relates to the Convertible Loan Notes (CLNs) and is lower owing to the extension of the CLN maturity date to 2025. The finance expense of £0.9m (H122: credit £2.4m) is a fair value adjustment of the derivative liability and not a cash item. This meant the reported loss before taxation was £4.1m (H122: profit £2.5m). R&D tax credits increased to £0.9m (H122: £0.7m) reflecting the higher level of development spend claimable in the period. Reported net loss was £3.2m (H122: profit £3.2m).

Cash resources in place to fund through to key milestones

Looking ahead, for FY23e we expect R&D spend to increase to £14.5m (FY22: £9.5m), as clinical trials progress and investment continues in the main technology platforms. We forecast G&A expenses to rise slightly to £5.3m (FY22: £4.8m). For FY24e we expect R&D to remain broadly stable at £15.1m, and G&A to continue to expand to £5.8m. We forecast a FY23e operating loss of £14.5m, and a wider loss of £20.9m in FY24e, with this owing to the non-recurring license income of £5.3m in FY23; conservatively, our financial forecasts do not include any future uncertain/unknown milestones from Genmab. Similarly, we forecast a FY23e net loss of £15.7m, and a wider loss of £21.9m in FY24e. We expect the FY23e cash position to be £17.8m at end-October 2023. We include an illustrative financing of £20m (as short-term debt) in FY24e, for end-October 2024 cash of £20.2m.

Successful execution and clinical delivery will determine share price performance

The next 12 months will be pivotal for Scancell. Progress of the novel and differentiated Moditope and ImmunoBody technology platforms, either into or through clinical development, or, in the case of the anti-glycan antibodies and AvidiMab platforms to convert into meaningful collaborations, should be key to unlocking shareholder value, as seen with the Genmab deal. Clinical disappointments, trial slippage, or a delay in executing attractive partnering deals will likely knock investor sentiment.

Exhibit 13: Summary of financials

Year-end: April 30	£'000s	2020	2021	2022	2023E	2024E
INCOME STATEMENT						
Revenues		**0**	**0**	**0**	**5,271**	**0**
Cost of goods sold		0	0	0	0	0
Gross Profit		**0**	**0**	**0**	**5,271**	**0**
R&D expenses		(4,667)	(6,406)	(9,477)	(14,504)	(15,144)
General and administrative expenses		(2,115)	(3,346)	(4,787)	(5,266)	(5,792)
Underlying operating profit		**(6,782)**	**(9,752)**	**(14,264)**	**(14,499)**	**(20,936)**
Other revenue/expenses		0	918	965	0	0
EBITDA		**(6,739)**	**(8,585)**	**(12,559)**	**(13,842)**	**(20,249)**
Operating Profit		**(6,782)**	**(8,834)**	**(13,299)**	**(14,499)**	**(20,936)**
Interest expense		14	(1,648)	(2,878)	(2,220)	(3,041)
Other financing costs/income		0	(6,323)	12,409	(910)	0
Profit Before Taxes		**(6,768)**	**(16,805)**	**(3,768)**	**(17,628)**	**(23,977)**
Adj. PBT		**(6,768)**	**(17,723)**	**(11,899)**	**(17,628)**	**(23,977)**
Current tax income		1,262	1,328	1,703	1,895	2,031
Cumulative preferred stock dividend		0	0	0	0	0
Net Income		**(5,506)**	**(15,477)**	**(2,065)**	**(15,733)**	**(21,947)**
EPS (p)		**(1.21)**	**(2.28)**	**(0.25)**	**(1.93)**	**(2.68)**
Adj. EPS (p)		**(1.21)**	**(2.42)**	**(1.25)**	**(1.93)**	**(2.68)**
DPS (p)		**0.00**	**0.00**	**0.00**	**0.00**	**0.00**
Average no. of shares (m)		456.2	678.6	815.2	815.9	818.4
Gross margin		*N/A*	*N/A*	*N/A*	*100%*	*N/A*
BALANCE SHEET						
Current assets		**5,208**	**44,668**	**32,362**	**21,156**	**23,500**
Cash and cash equivalents		3,575	41,110	28,725	17,766	20,160
Accounts receivable		371	968	647	400	350
Inventories		0	0	0	0	0
Other current assets		1,262	2,590	2,990	2,990	2,990
Non-current assets		**3,610**	**4,390**	**6,159**	**5,702**	**5,215**
Property, plant & equipment		195	975	2,744	2,287	1,800
Other non-current assets		0	0	0	0	0
Current liabilities		**(1,091)**	**(2,295)**	**(2,452)**	**(3,980)**	**(24,476)**
Short-term debt		0	0	0	0	(20,000)
Accounts payable		(1,041)	(2,087)	(2,137)	(3,665)	(4,161)
Other current liabilities		(50)	(208)	(315)	(315)	(315)
Non-current liabilities		**(79)**	**(27,278)**	**(17,959)**	**(19,909)**	**(19,659)**
Long-term debt		0	(27,215)	(17,103)	(19,303)	(19,303)
Other non-current liabilities		(79)	(63)	(856)	(606)	(356)
Equity		**7,648**	**19,485**	**18,110**	**2,969**	**(15,420)**
Share capital		38,853	65,834	65,834	65,977	65,977
Other		(31,205)	(46,349)	(47,724)	(63,008)	(81,397)
CASH FLOW STATEMENTS						
Operating cash flow		**(4,772)**	**(7,803)**	**(10,730)**	**(9,900)**	**(17,245)**
Profit before tax		(6,768)	(16,805)	(3,768)	(17,628)	(23,977)
Non-cash adjustments		22	8,553	(8,101)	4,786	4,828
Change in working capital		143	449	372	1,775	545
Interest paid		0	0	(537)	(537)	(537)
Taxes paid		1,831	0	1,304	1,703	1,895
Investing cash flow		**(13)**	**(741)**	**(1,264)**	**(42)**	**(111)**
CAPEX on tangible assets		(27)	(744)	(1,268)	(200)	(200)
Other investing cash flows		14	3	4	158	89
Financing cash flow		**3,800**	**46,079**	**(391)**	**(107)**	**19,750**
Proceeds from equity		3,827	22,727	0	143	0
Increase in loans		0	23,506	0	0	20,000
Other financing cash flow		(27)	(154)	(391)	(250)	(250)
Net increase in cash		**(985)**	**37,535**	**(12,385)**	**(10,959)**	**2,394**
Cash at start of year		4,560	3,575	41,110	28,725	17,766
Cash at end of year		**3,575**	**41,110**	**28,725**	**17,766**	**20,160**
Net cash at end of year		3,575	13,895	11,622	(1,537)	(19,143)

Source: Company, Trinity Delta Note: Adjusted numbers exclude exceptionals.

Company information

Contact details

Scancell,
Unit 202 Bellhouse Building
Sanders Road,
Oxford Science Park,
Oxford,
OX4 4GD, UK

Tel: +44 (0) 1865 582 066

Web: www.scancell.co.uk

Key personnel

Person	Position	Biography
Dr Jean-Michel Cosséry	Non-Executive Chair	Joined as Chair in February 2023. 25+ years of pharma and biotech experience, including commercial opertions, capital raising, IPOs, business development and M&A. Previously, VP North America Oncology at Eli Lilly, Chair of the Eli Lilly UK Board, and Chief Marketing Officer at GE Healthcare. Current NED at Malin Plc, Exact Therapeutics, Eracal Therapeutics, and Sophia Genetics; prior NED at Kymab, Immunocore.
Professor Lindy Durrant	CEO	Founded Scancell in January 1996 as a spin-out from her work at the University of Nottingham (which she joined in December 1983). Initially Co-CEO then CSO before becoming CEO in July 2021. Also Professor of Cancer Immunology at the Department of Clinical Oncology. Over 200 publications in peer-reviewed journals and over 143 patents filed. Holds BSc (Hons) Biochemistry and a PhD from Manchester University.
Dr Sally Adams	CDO	Joined Scancell in May 2014 as Development Director. Wide ranging experience, with nearly 30 years experience in drug development including 11 years as Director of Immunotherapeutics at British Biotech. Holds a MA Genetics from the University of Cambridge and a PhD in Microbiology from Imperial College London.

Top shareholdings

	% holding
Redmile Group	29.37
Vulpes Life Science Fund	14.39
Calculus Capital	4.58
Scancell directors and related holdings	1.24
Top institutional investors	**47.58**
Other shareholders	52.42
Total shareholders	**100.00**

Source: Scancell

Philippa Gardner pgardner@trinitydelta.org +44 (0) 20 3637 5042

Lala Gregorek lgregorek@trinitydelta.org +44 (0) 20 3637 5043

Franc Gregori fgregori@trinitydelta.org +44 (0) 20 3637 5041

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